less than that of bond lengths as a result of the influence of thermal motion (Domenicano, Vaciago & Coulson, 1975), the effect on the C8—C9 distance is less significant than that on the C10—C9—C14 bond angle; this value [118.8 (2)°] is lower than 120° suggesting some π-electron delocalization with the —C=N—OH substituent.

The crystal-packing diagram shows distinctly the strong hydrogen bonds between oxime and carboxyl groups related by the *n*-glide plane. The O2—HO2···N1 hydrogen bond has a length of 2.718 (2) Å with an angle of 174 (3)° while the O1···HO3—O3 hydrogen bond has a length 2.720 (2) Å and an angle of 157 (3)°. The mentioned hydrogen bonds have intermediate values compared with those observed in several oxime–oxime dimers (Bachechi & Zambonelli, 1972, 1973; Brehm & Watson, 1972; Gieren, Huebner & Ruiz-Perez, 1986) and those determined in carboxylic acid dimers [see for example Patil, Curtin & Paul (1985)]. No other hydrogen bonds or close intermolecular contacts were observed.

We thank the National Science Foundation (USA) for support of this work through grant CHE 85-10600.

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Structures of Three Derivatives of 6-Phthalimidopenicillanic Acid

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(*Received* 17 *December* 1990; *accepted* 3 *March* 1992)

Abstract. *cis*-6-Phthalimidopenicillanic acid, methyl ester, $C_{17}H_{16}N_2O_5S$ (*A*), $M_r = 360.39$, monoclinic, $P2_1$, $a = 11.137$ (2), $b = 6.976$ (4), $c = 11.755$ (3) Å, $\beta = 111.57$ (1)°, $V = 849$ (1) Å^3, $Z = 2$, $D_x = 1.412$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.71069 Å, $\mu = 0.2107$ mm^{-1}, $F(000) = 376$, $T = 298$ K, final $R = 0.030$ for 1457 unique diffractometer data and 225 refined parameters. *trans*-6-Phthalimidopenicillanic acid, methyl ester, $C_{17}H_{16}N_2O_5S$ (*B*), $M_r = 360.39$, orthorhombic, $P2_12_12_1$, $a = 10.276$ (2), $b = 10.850$ (2), $c = 15.371$ (3) Å, $V = 1713.8$ (6) Å^3, $Z = 4$, $D_x = 1.397$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.71069 Å, $\mu = 0.2107$ mm^{-1}, $F(000) = 752$, $T = 298$ K, final $R = 0.045$ for 1232 unique diffractometer data and 225 refined parameters. *cis*-6-Phthalimidopenicillanic acid, α-sulfoxide monohydrate, $C_{16}H_{14}N_2O_6S.H_2O$ (*C*), $M_r = 380.35$, orthorhombic, $P2_12_12_1$, $a = 10.028$ (2), $b = 13.004$ (3), $c = 12.865$ (2) Å, $V = 1677.5$ (6) Å^3, $Z = 4$, $D_x = 1.506$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.71069 Å, $\mu = 0.2200$ mm^{-1}, $F(000) = 792$, $T = 298$ K, final $R = 0.043$ for 1432 unique diffractometer data and 235 refined parameters. Twist (*T*), envelope E_3, and envelope E_S conformations have been observed for the thiazolidine ring of *A*, *B* and *C*, respectively. Epimerization at C atom C6 does not change the pyramidality of the β-lactam N atom; however, the β-lactam ring is more planar and the overall topology of the molecule is altered. Oxidation of the S atom to sulfoxide diminished pyramidality of the N atom and provided a very good acceptor for hydrogen bonding [O—H···O distance 2.633 (5) Å]. For the *cis* β-lactams *A* and *C*, short intramolecular non-bonding distances between the S atom and atoms from thiazolidine substitutents were observed. The relative orientation of the carboxyl group at C3

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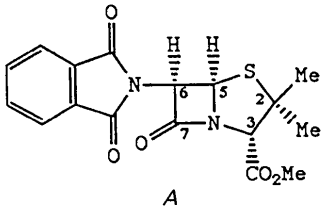
0108-2701/92/122167-06$06.00

with respect to the C3, C5, C7 least-squares plane is different in the methyl ester (*A* and *B*) and free acid forms (*C*).

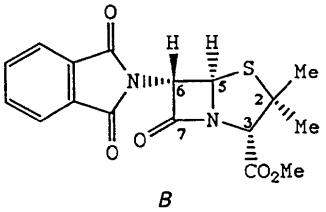
Introduction. Since the discovery of the therapeutic potential of penicillin, more than 80 crystal structures of bioactive compounds of the penicillin family have been reported over the last few decades (Cambridge Structural Database, 1990). Structural studies revealed some features of this rather strained molecule containing a fused four-membered β-lactam ring and a five-membered thiazolidine ring. Pyramidality of the β-lactam N atom, the shape of the thiazolidine ring which affects the configuration of the carboxyl group at C atom C3, and the conformation of the substituent at C atom C6 are usually considered to be factors influencing the antibiotic action of penicillins. Although highly potent penicillins have been discovered and are in wide use, pharmacologists and medicinal chemists are not yet able to correlate in detail the chemical and biological nature of this most powerful drug of the 20th Century (Frère, Joris, Varetto & Crine, 1988).

In order to understand better the influence of such factors as epimerization at C6, oxidation of the S atom or esterification of the carboxyl group, on the topology of the ring system, crystal structures of the following compounds have been solved:



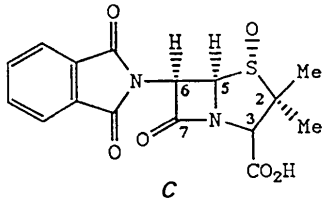
A

cis-6-Phthalimidopenicillanic acid, methyl ester



B

trans-6-Phthalimidopenicillanic acid, methyl ester



C

cis-6-Phthalimidopenicillanic acid, α-sulfoxide (monohydrate)

Experimental. Compound *A* was prepared according to the procedure described by Sheehan & Henery-Logan (1962) and converted to *B* by epimerization (Wolfe & Lee, 1968) at C6, while compound *C* was obtained by oxidation of the carboxylic acid corresponding to *A* (methyl ester) with ozone (Spry, 1972).

Crystals of *A* and *C* were obtained by slow evaporation of CH_2Cl_2/hexane solution. Crystals of compound *B* growing in clusters were recrystallized from CH_2Cl_2 with a small amount of silica gel (200–400 mesh) at the bottom of the crystallization flask in order to separate individual crystals from one another. A crystal growing partially in the gel and partially in the solution was selected for X-ray studies. Crystal sizes: *A* 0.17 × 0.17 × 0.35 mm; *B* 0.15 × 0.15 × 0.52 mm; *C* 0.28 × 0.42 × 0.52 mm. Cell dimensions were obtained at 298 K from least-squares refinement of 25 reflections in the 2θ ranges: *A* 9.8–29.4°, *B* 8.0–21.2°, *C* 14.0–24.0°. An Enraf–Nonius CAD-4 diffractometer with monochromated Mo $K\alpha$ radiation and 2θ scan was used for data collection ($2\theta_{max} = 50°$); *hkl* ranges: *A* 0–13, 0–8, 0 ± 14; *B* 0–12, 0–12, 0–18; *C* 0–11, 0–13, 0–14. In all cases three standards monitored every hour showed only ±1% random variations during data collection. Of the 1606, 1737 and 1763 reflections measured, 1457, 1232 and 1432 with $I > 3\sigma(I)$ were considered as observed, for *A*, *B* and *C*, respectively. Intensities were corrected for Lp, ψ-scan-based absorption for *B* (minimum and maximum correction 0.86 and 0.99), and numerical absorption at isotropic level of refinement for *C* (minimum and maximum corrections 0.91 and 0.96) using *DIFABS* (Walker & Stuart, 1983).

Structures were solved by direct methods (*SHELXS*86; Sheldrick, 1986) and refined by full-matrix least-squares minimizing $\sum w(\Delta F)^2$ where $w = 1/[\sigma(F)^2 + (0.02F)^2 + 1]$ and σ was obtained from counting statistics. C5, C6 and carboxyl H atoms were found from ΔF syntheses and refined for six cycles only, with damping factor 0.5 and *B* factor kept at a constant value of 6 Å^2; otherwise, atomic parameters were recalculated after every three cycles of refinement. The final cycles of refinement gave: compound *A* $R = 0.030$, $wR = 0.038$ (225 parameters and 1457 F_o); compound *B* $R = 0.045$, $wR = 0.047$ (225 and 1232 F_o); compound *C* $R = 0.043$, $wR = 0.053$ (235 parameters and 1432 F_o). The goodness-of-fit values were 1.008, 1.015 and 1.203 for *A*, *B* and *C*, respectively. $(\Delta/\sigma)_{max}$ was 0.15 for *A*, 0.09 for *B* and 0.09 for *C*. No fluctuation in electron density on final ΔF maps above 0.17 e Å^{-3} for *A*, 0.27 e Å^{-3} for *B* and 0.22 e Å^{-3} for *C* were observed, although two H atoms from the water molecule of *C* were not found. All calculations (except structure solution) and drawings were made with the Enraf–

Table 1. *Fractional coordinates and equivalent isotropic thermal parameters* (Å^2)

$$B_{eq} = (4/3)[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)].$$

	x	*y*	*z*	B_{eq}
Compound *A*				
S1	0.6881 (1)	0.545*	0.0334 (1)	3.26 (2)
C2	0.7398 (4)	0.4766 (8)	−0.0951 (4)	2.92 (9)
C3	0.6776 (4)	0.2743 (8)	−0.1397 (4)	2.97 (9)
N4	0.6553 (3)	0.1849 (6)	−0.0385 (3)	3.06 (8)
C5	0.6200 (4)	0.3108 (8)	0.0438 (4)	3.1 (1)
C6	0.6914 (4)	0.1686 (8)	0.1487 (4)	3.3 (1)
C7	0.7422 (4)	0.0760 (7)	0.0555 (4)	3.3 (1)
C8	0.8872 (4)	0.459 (1)	−0.0465 (4)	4.1 (1)
C9	0.6955 (5)	0.6337 (9)	−0.1920 (4)	4.3 (1)
C10	0.5514 (4)	0.2807 (8)	−0.2481 (3)	3.15 (9)
O11	0.4474 (3)	0.2953 (8)	−0.2418 (3)	4.59 (9)
O12	0.5708 (3)	0.2667 (7)	−0.3530 (2)	4.33 (8)
C13	0.4555 (5)	0.273 (1)	−0.4625 (4)	5.5 (2)
O14	0.8170 (4)	−0.0451 (6)	0.0532 (3)	4.40 (8)
N15	0.7828 (3)	0.2277 (6)	0.2660 (3)	3.06 (8)
C16	0.9175 (4)	0.2460 (8)	0.2998 (4)	3.12 (9)
C17	0.9692 (4)	0.2586 (7)	0.4359 (4)	3.17 (9)
C18	1.0952 (4)	0.2634 (8)	0.5178 (4)	3.7 (1)
C19	1.1162 (5)	0.2607 (9)	0.6414 (5)	4.4 (1)
C20	1.0135 (5)	0.257 (1)	0.6811 (4)	4.6 (1)
C21	0.8874 (5)	0.2534 (9)	0.5993 (4)	4.0 (1)
C22	0.8676 (4)	0.2530 (8)	0.4761 (3)	3.18 (9)
C23	0.7471 (4)	0.2353 (8)	0.3681 (4)	3.5 (1)
O24	0.9743 (3)	0.2489 (6)	0.2309 (3)	4.18 (8)
O25	0.6374 (3)	0.2237 (8)	0.3629 (3)	5.4 (1)
Compound *B*				
S1	0.0660 (2)	0.9441 (1)	0.48936 (9)	5.91 (3)
C2	0.1664 (5)	0.8909 (5)	0.5812 (3)	4.3 (1)
C3	0.1800 (4)	1.0080 (4)	0.6415 (3)	3.61 (9)
N4	0.1866 (4)	1.1119 (4)	0.5828 (2)	3.68 (8)
C5	0.1047 (5)	1.1066 (5)	0.5053 (3)	4.2 (1)
C6	0.2189 (5)	1.1628 (4)	0.4519 (3)	3.7 (1)
C7	0.2950 (5)	1.1565 (4)	0.5392 (3)	3.8 (1)
C8	0.3036 (6)	0.8547 (5)	0.5523 (4)	5.3 (1)
C9	0.0961 (6)	0.7824 (5)	0.6229 (4)	5.7 (1)
C10	0.0670 (5)	1.0249 (5)	0.7032 (3)	4.2 (1)
O11	−0.0271 (4)	1.0872 (4)	0.6893 (3)	6.45 (9)
O12	0.0835 (3)	0.9554 (3)	0.7741 (2)	5.01 (8)
C13	−0.0269 (6)	0.9430 (6)	0.8326 (3)	6.5 (1)
O14	0.4045 (3)	1.1737 (3)	0.5621 (2)	4.76 (8)
N15	0.2035 (4)	1.2787 (4)	0.4078 (2)	3.54 (8)
C16	0.2046 (5)	1.3935 (5)	0.4472 (3)	4.0 (1)
C17	0.1769 (4)	1.4833 (4)	0.3757 (3)	3.8 (1)
C18	0.1691 (6)	1.6089 (5)	0.3772 (4)	6.0 (1)
C19	0.1448 (6)	1.6681 (5)	0.2971 (4)	6.6 (2)
C20	0.1265 (6)	1.6033 (6)	0.2229 (4)	6.2 (1)
C21	0.1330 (5)	1.4763 (6)	0.2217 (3)	5.2 (1)
C22	0.1579 (4)	1.4169 (5)	0.2996 (3)	3.8 (1)
C23	0.1729 (4)	1.2853 (5)	0.3207 (3)	3.8 (1)
O24	0.2246 (4)	1.4136 (3)	0.5232 (2)	5.41 (9)
O25	0.1619 (4)	1.1963 (3)	0.2731 (2)	5.17 (8)
Compound *C*				
S1	0.9973 (1)	0.80648 (9)	0.82706 (9)	2.45 (2)
C2	0.9344 (5)	0.9275 (4)	0.7615 (4)	2.6 (1)
C3	0.8193 (5)	0.9666 (4)	0.8327 (4)	2.51 (9)
N4	0.8463 (4)	0.9249 (3)	0.9360 (3)	2.61 (8)
C5	0.9661 (5)	0.8666 (4)	0.9538 (4)	2.37 (9)
C6	0.8899 (5)	0.8092 (4)	1.0421 (3)	2.42 (9)
C7	0.7658 (5)	0.8662 (4)	1.0009 (4)	2.4 (1)
C8	1.0517 (6)	1.0013 (4)	0.7546 (5)	3.8 (1)
C9	0.8861 (7)	0.8941 (5)	0.6546 (4)	4.9 (2)
C10	0.8157 (5)	1.0831 (4)	0.8353 (4)	2.9 (1)
O11	0.8559 (6)	1.1348 (3)	0.9050 (3)	5.4 (1)
O12	0.7697 (4)	1.1202 (3)	0.7466 (3)	3.62 (8)
O13	1.1449 (3)	0.8037 (3)	0.8076 (3)	2.94 (7)
O14	0.6481 (3)	0.8669 (3)	1.0158 (3)	3.12 (7)
N15	0.8837 (4)	0.7002 (3)	1.0478 (3)	2.34 (7)
C16	0.8104 (5)	0.6382 (4)	0.9803 (4)	2.7 (1)
C17	0.8186 (5)	0.5328 (4)	1.0217 (4)	2.8 (1)
C18	0.7667 (6)	0.4420 (5)	0.9859 (4)	4.0 (1)
C19	0.7921 (7)	0.3537 (5)	1.0433 (5)	5.0 (2)
C20	0.8634 (8)	0.3562 (5)	1.1333 (6)	6.2 (2)
C21	0.9162 (7)	0.4483 (5)	1.1723 (5)	4.9 (1)
C22	0.8937 (6)	0.5359 (4)	1.1134 (4)	3.5 (1)
C23	0.9342 (5)	0.6453 (4)	1.1334 (4)	3.1 (1)
O24	0.7534 (4)	0.6694 (3)	0.9047 (3)	3.42 (8)
O25	0.9925 (4)	0.6812 (3)	1.2055 (3)	4.37 (8)
O26	0.5469 (8)	0.9388 (6)	0.6098 (5)	10.9 (2)

* Coordinate fixed to define origin of structure with non-centrosymmetric space group.

Table 2. *Bond distances* (Å)

	Compound *A*	Compound *B*	Compound *C*
S1—C2	1.866 (5)	1.841 (5)	1.894 (5)
S1—C5	1.823 (6)	1.825 (5)	1.835 (5)
C2—C3	1.575 (7)	1.579 (7)	1.559 (7)
C2—C8	1.532 (6)	1.530 (8)	1.520 (7)
C2—C9	1.526 (7)	1.523 (8)	1.521 (7)
C3—N4	1.444 (6)	1.446 (6)	1.461 (6)
C3—C10	1.512 (5)	1.510 (6)	1.515 (7)
N4—C5	1.463 (7)	1.458 (6)	1.439 (6)
N4—C7	1.396 (5)	1.387 (6)	1.390 (6)
C5—C6	1.555 (6)	1.557 (7)	1.560 (6)
C6—C7	1.548 (7)	1.555 (6)	1.543 (7)
C6—N15	1.441 (5)	1.437 (6)	1.421 (6)
C7—O14	1.193 (6)	1.194 (6)	1.196 (6)
C10—O11	1.192 (6)	1.199 (6)	1.192 (6)
C10—O12	1.332 (5)	1.336 (6)	1.321 (6)
O12—C13	1.447 (5)	1.454 (6)	–
N15—C16	1.409 (5)	1.385 (6)	1.394 (6)
N15—C23	1.397 (6)	1.377 (6)	1.406 (6)
C16—C17	1.490 (6)	1.496 (6)	1.472 (7)
C16—O24	1.197 (6)	1.207 (5)	1.199 (6)
C17—C18	1.380 (5)	1.365 (7)	1.370 (8)
C17—C22	1.377 (7)	1.387 (6)	1.400 (7)
C18—C19	1.385 (7)	1.411 (9)	1.389 (9)
C19—C20	1.385 (9)	1.353 (9)	1.36 (1)
C20—C21	1.380 (6)	1.379 (9)	1.402 (9)
C21—C22	1.383 (6)	1.385 (7)	1.387 (8)
C22—C23	1.475 (5)	1.472 (7)	1.501 (8)
C23—O25	1.204 (6)	1.217 (6)	1.191 (6)
S1—O13	–	–	1.502 (4)

Nonius (1979) *SDP* system on a MicroVAX II computer. Atomic scattering factors were used as supplied in the *SDP* system.

Discussion. Atomic positions and equivalent isotropic temperature factors for compounds *A*, *B* and *C* are listed in Table 1,* selected interatomic distances are given in Table 2, and bond angles in Table 3.

As shown in the *PLUTO* (Motherwell & Clegg, 1978) diagrams (Fig. 1), the molecular shape could be approximated by the shape of an open book (with β-lactam N and C5 atoms located at the spine of the book). Analysis of bond lengths and bond angles shows elongation of C2—C3, N4—C7 and C5—C6 bonds but reduction in the C7=O14 distance when compared to the bond lengths of 1-aza-2-cyclobutanone, solved at 170 K (Yang, Seiler & Dunitz, 1987), reflecting the influence of ring fusion on the molecular geometry. On the other hand, these bond lengths are very close to those obtained by Wolfe, Khalil & Weaver (1988) by averaging bond distances from eight penicillin molecules, during a search for geometrical parameters for *MMP*2 calculations.

The shape of the thiazolidine ring was investigated in terms of the magnitudes and symmetry of distribution of torsion angles [asymmetry parameters of Duax, Weeks & Rohrer (1976)]. As shown in Fig. 2, molecules *A*, *B* and *C* have markedly different sym-

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55342 (55 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. *Bond angles* (°)

	Compound *A*	Compound *B*	Compound *C*
C2—S1—C5	94.9 (2)	94.6 (3)	89.2 (3)
S1—C2—C3	105.6 (3)	104.3 (4)	104.8 (3)
S1—C2—C8	109.0 (3)	112.0 (4)	107.0 (3)
S1—C2—C9	108.0 (4)	107.4 (4)	105.7 (4)
C3—C2—C8	109.3 (4)	107.0 (5)	113.7 (4)
C3—C2—C9	114.4 (3)	114.6 (5)	112.8 (5)
C8—C2—C9	110.3 (4)	111.4 (5)	112.0 (5)
C2—C3—N4	107.5 (3)	105.4 (4)	106.0 (4)
C2—C3—C10	114.4 (4)	113.4 (4)	110.9 (4)
N4—C3—C10	108.6 (4)	109.1 (4)	110.8 (4)
C3—N4—C5	117.1 (4)	117.0 (4)	119.7 (4)
C3—N4—C7	127.4 (4)	127.5 (4)	130.0 (4)
C5—N4—C7	94.6 (3)	94.7 (4)	95.7 (4)
S1—C5—N4	105.9 (3)	105.7 (4)	103.0 (3)
S1—C5—C6	121.3 (3)	118.0 (4)	121.8 (3)
N4—C5—C6	87.6 (4)	89.0 (4)	87.7 (3)
C5—C6—C7	85.3 (3)	84.7 (4)	85.1 (3)
C5—C6—N15	123.5 (4)	120.5 (4)	122.4 (4)
C7—C6—N15	118.9 (4)	119.8 (4)	117.5 (4)
N4—C7—C6	90.3 (4)	91.6 (4)	90.1 (4)
N4—C7—O14	130.9 (5)	131.9 (5)	131.8 (4)
C6—C7—O14	138.7 (4)	136.3 (5)	138.1 (4)
C3—C10—O11	125.1 (4)	125.5 (5)	125.0 (5)
C3—C10—O12	111.1 (4)	109.9 (4)	110.7 (4)
O11—C10—O12	123.8 (3)	124.4 (5)	124.2 (5)
C10—O12—C13	115.4 (4)	117.1 (4)	–
C6—N15—C16	126.9 (4)	125.4 (4)	124.6 (4)
C6—N15—C23	120.6 (4)	121.8 (4)	122.1 (4)
C16—N15—C23	111.3 (3)	112.5 (4)	112.6 (4)
N15—C16—C17	105.1 (4)	105.2 (4)	106.4 (4)
N15—C16—O24	125.7 (3)	126.0 (5)	124.1 (5)
C17—C16—O24	129.3 (4)	128.8 (5)	129.4 (5)
C16—C17—C18	130.0 (5)	130.2 (5)	131.2 (5)
C16—C17—C22	108.9 (3)	107.9 (5)	108.0 (4)
C18—C17—C22	120.9 (4)	121.9 (5)	120.8 (5)
C17—C18—C19	117.9 (5)	116.4 (6)	117.7 (5)
C18—C19—C20	120.8 (4)	121.8 (6)	121.9 (6)
C19—C20—C21	121.4 (4)	121.4 (6)	121.6 (6)
C20—C21—C22	117.4 (5)	117.4 (5)	116.4 (6)
C17—C22—C21	121.6 (4)	121.0 (5)	121.6 (5)
C17—C22—C23	108.0 (4)	107.8 (4)	108.5 (4)
C21—C22—C23	130.3 (5)	131.1 (5)	129.9 (5)
N15—C23—C22	106.6 (4)	106.5 (4)	104.5 (4)
N15—C23—O25	123.9 (3)	124.5 (5)	126.0 (5)
C22—C23—O25	129.4 (4)	129.0 (5)	129.6 (5)
C2—S1—O13	–	–	105.9 (2)
C5—S1—O13	–	–	109.0 (2)

metry of the intracyclic torsion-angle distribution. The *cis* isomer (*A*) adopts a twist (*T*) conformation with twofold symmetry. The *trans* isomer (*B*) and *cis* sulfoxide (*C*) adopt envelope E_3 and E_S conformations, respectively. In these rings, a plane is the dominating element of symmetry. The E_3 and E_S conformations are considered to be the two standard shapes of the thiazolidine ring of the penicillin system with the 2β-CH_3 and C3-carboxyl groups nearly diaxial in one (*B*), and both groups nearly diequatorial in the other (*C*) (Blanpain, Nagy, Laurent & Durant, 1980). Asymmetry parameters (Duax, Weeks & Rohrer, 1976) for the thiazolidine ring in compounds *A*, *B* and *C* are $\Delta C_2(S1) = 1.9\ (9)°$, $\Delta C_s(C3) = 2\ (1)°$ and $\Delta C_s(S1) = 4.5\ (9)°$, respectively. The phthalimido group at C6 is planar and in all the above molecules is almost perpendicular to the plane of the β-lactam ring.

We chose the C3, C5, C7 plane as a reference for describing molecular conformation. Table 4 gives distances between this plane and prospective active centers during penicillin molecule–binding site interactions. It shows that epimerization at the C6 center does not change the pyramidality of N4, contrary to S-atom oxidation to sulfoxide in *C*. Epimerization at C6, however, along with higher planarity of the β-lactam ring (see Fig. 2), changes the molecular shape, and probably thus reduces access of the β-lactam N atom for interactions with an active site. Despite different conformations of the thiazolidine ring, the S1 and N4 atoms are always located on opposite sides of the C3, C5, C7 plane. Deviations of

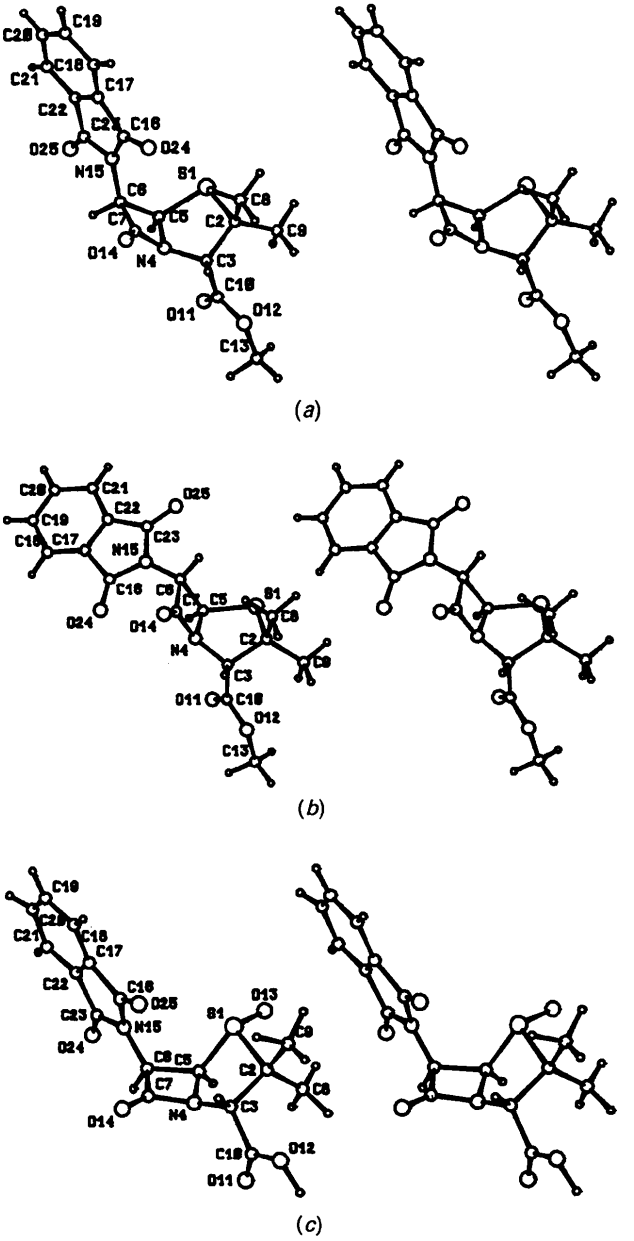


Fig. 1. *PLUTO* (Motherwell & Clegg, 1983) diagrams showing in stereo the conformations of the molecules of compounds *A*, *B* and *C*.

polar atoms from the above plane suggest that distributions of electronegative and electropositive regions on the active surface of these molecules are slightly different.

Critical for recognition of penicillin molecules by D,D-carboxypeptidase-transpeptidase or β-lactamase is the location and orientation of the C3 carboxyl group (Gale, Cundliffe, Reynolds, Richmond & Waring, 1981). As shown in Table 4, the distance of C10 from the reference plane is not much different in the three isomers. Despite the fact that the carboxyl group at C3 is axial in *A* and *B* and equatorial in *C*, one O atom (C=O) is located at a distance of *ca* 1 Å and the other at a distance of *ca* 2–2.3 Å from the above plane. Moreover, in molecule *C*, a very short contact between the β-lactam N atom and the O atom from the carboxyl group (C=O) was found [2.761 (3) Å; not observed in *A* and *B*] showing that the relative orientation of the COO^- group with respect to the above plane can be different, for example, under the influence of hydration. Recently, the crystal structures of two natural targets for

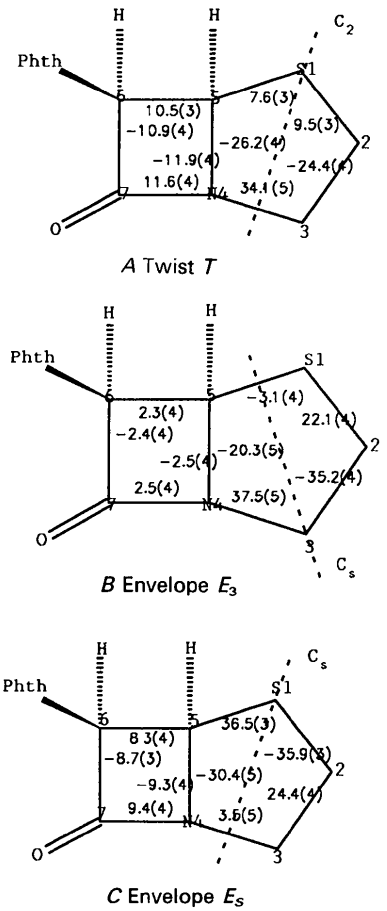


Fig. 2. Intracyclic torsion angles (°) and conformations in molecules of compounds *A*, *B* and *C*.

Table 4. *Distances of selected atoms* (Å) *from the* C3, C5, C7 *plane*

		Compound *A*	Compound *B*	Compound *C*
N4		−0.375 (4)	−0.375 (4)	−0.308 (3)
S1		1.466 (1)	1.351 (2)	1.474 (1)
C10	(COO^-)	−1.121 (5)	−1.053 (5)	−1.265 (5)
O11	(C=O)	−1.853 (4)	−1.805 (5)	−2.370 (4)
O12	(C—O^-)	−1.197 (4)	−0.986 (4)	−0.976 (3)

β-lactams – *A*-class β-lactamase from *Staphylococcus aureus* (Herzberg & Moult, 1987) and D,D-carboxypeptidase from *Streptomyces R*61 – with three different β-lactam molecules diffused into the crystal (Kelly, Knox, Zhao, Frère & Ghuysen, 1989) were solved. Modelling of these β-lactam molecules and fitting their cleavage products in the binding site of an enzyme strongly confirms their attack on the α-face of β-lactams, thus suggesting the primary importance of such factors such as accessibility of the β-lactam N atom, relative locations of all groups allowing hydrogen-bond formation, or hydrophobic interactions with the receptor. The fact that both hydrophobic and hydrophilic residues at C6 can be located in the same area of the binding site of the *R*61 D,D-carboxypeptidase (Kelly, Knox, Zhao, Frère & Ghuysen, 1989) shows that these interactions are less specific than the former.

Characteristic features of the penicillin molecules in *cis* configuration are numerous short intramolecular contacts between the S atom and atoms from the substituent at C6. Among them, the distances between S1 and N15 [3.371 (4) and 3.358 (4) Å in compounds *A* and *C*, respectively], and S1 and O24 from the phthalimido group [3.185 (5) Å] are the shortest.

Monohydrate *C*, possessing a free carboxyl group, has a very extensive hydrogen-bond pattern: carboxyl O atom O12 forms a rather short hydrogen bond [2.633 (5) Å] with the O atom from the S=O group. The water molecule of solvation has two short contacts with O25 from the phthalimido group [2.893 (4) Å] and O11 from the carboxyl group [2.967 (5) Å].

We are grateful to Professor A. K. Bose for encouragement and stimulating discussions, Dr Z. Kaluza for synthesis of our model compounds, and Stevens Institute of Technology and Howard Hughes Medical Institute for research facilities and financial support.

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Structure of Methyl 3-Benzyl-5-phenyl-3*H*-1,2,4-dioxazole-3-carboxylate

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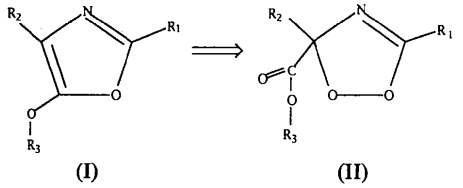
(*Received* 30 *November* 1991; *accepted* 6 *April* 1992)

Abstract. $C_{17}H_{15}NO_4$, $M_r = 297.3$, monoclinic, $C2/c$, $a = 26.157\ (5)$, $b = 5.979\ (1)$, $c = 19.492\ (3)$ Å, $\beta = 97.79\ (1)°$, $V = 3020\ (1)$ Å^3, $Z = 8$, $D_x = 1.31$ g cm^{-3}, λ(Cu $K\alpha$) = 1.5418 Å, $\mu = 7.36$ cm^{-1}, $F(000) = 1248$, room temperature, final $R = 0.058$ for 1545 independent reflections and 199 parameters. The five-membered heterocyclic ring shows an envelope conformation where one of the two peroxy O atoms occupies the apical position. The out-of-plane displacement is particularly small in relation to the valence state of the peroxy O atoms.

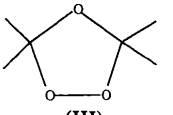
Introduction. Studies of oxidation with singlet molecular oxygen of 5-alkoxyoxazoles (I) have shown that, in favourable conditions, they are partly converted into 3-alkoxycarbonyl-1,2,4-dioxazoles (II) (Graziano, Iesce, Carotenuto & Scarpati, 1977*a*,*b*).



(I) (II)

The structure (II) was assigned on the basis of elemental and spectral data. To confirm the structure assignment, X-ray analysis of the title compound, where $R_1 = C_6H_5$, $R_2 = CH_2C_6H_5$ and $R_3 = CH_3$, has been carried out. This is the first X-ray characterization of this new heterocyclic system.

It is worth comparing the conformation of the dioxazole ring with that of trioxolane ring (III) as found in the structure of *trans*-5-[3,3-bis(methoxycarbonyl)-2-oxiranyl]-3-[2,2-bis(methoxycarbonyl)vinyl]-3,5-diphenyl-1,2,4-trioxolane (Giordano & Cermola, 1990).



(III)

Here the trioxolane ring exhibits a perfect envelope conformation with a pseudo-C_s symmetry. One of the two adjacent peroxy O atoms is displaced by 0.657 (3) Å out of the plane formed by the other four intra-ring atoms. The relevant puckering of the ring has been ascribed to the need to stagger the electron lone pairs on the two adjacent O atoms, which appear to be in the sp^3-hybridized state.

Experimental. A prismatic crystal (0.2 × 0.3 × 0.5 mm), elongated along **b**, was used for data collection on an Enraf–Nonius CAD-4 automatic diffractometer with graphite-monochromated Cu $K\alpha$ radiation. The unit-cell parameters and orientation matrix were obtained by a least-squares fitting of the setting angles of 25 reflections ($18 \le \theta \le 27°$). Out of 3146 independent reflections measured by the ω/θ scan technique with $\theta \le 75°$, 1545 having $I_o > 3\sigma(I_o)$ were used in the structure determination ($-32 \le h \le$

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